

CLAIMS:RELEASED BY  
ART 34 AMB

1. A method for assessing the tolerogenicity of a test peptide sequence from an infectious agent, comprising the steps of:

(i) contacting a cell population with said test peptide sequence,

(ii) determining whether IL-10 expression in said cell population is increased, and optionally

(iii) correlating the result of step (ii) with the tolerogenicity of the sequence,

wherein said cell population comprises mononuclear leukocytes from a donor previously infected by said infectious agent.

2. A method according to claim 1, wherein said cell population comprises at least one type of antigen presenting cell.

3. A method according to claim 1 or claim 2, wherein said mononuclear leukocytes comprise at least T lymphocytes, B lymphocytes, natural killer (NK) cells, monocytes, macrophages or dendritic cells.

4. A method according to claim 3, wherein said mononuclear leukocytes comprise at least CD4<sup>+</sup> T lymphocytes.

5. A method according to claim 4, wherein said mononuclear leukocytes further comprise at least one type of antigen presenting cell.

6. A method according to any one of claims 1 to 5, further comprising the steps of:

(i) (a) contacting a similar cell population from a donor not previously infected by said infectious agent with said test peptide sequence; and

(ii) (a) determining whether IL-10 expression in said cell population is increased,

and optionally

(ii) (b) comparing the results from step (ii) with the results from step (ii) (a).

7. A method according to any one of claims 1 to 6, wherein the infectious agent is a virus.

8. A method according to claim 7, wherein the virus is a herpesvirus encoding a viral IL-10 homologue

9. A method according to claim 8, wherein the virus is EBV.

10. A method according to claim 9, wherein the test peptide sequence is derived from EBV LMP1 protein or LMP2 protein.

11. A method according to claim 10, wherein the test or tolerogenic peptide sequence comprises one or more of the sequences P1 to P75 or P1' to P96'.

12. A method for assessing the tolerogenicity of a test peptide sequence from an infectious agent towards a target antigen, comprising the steps of:

(i) contacting a cell population with (a) said test peptide sequence and (b) a target antigen, to make a test composition, and

(ii) re-contacting the cell population from said test composition with said target antigen.

wherein said cell population comprises mononuclear leukocytes from a donor previously infected by said infectious agent.

21. A method according to claim 20, wherein the test or tolerogenic peptide sequence comprises one or more of the sequences P1 to P75 or P1' to P96'.

22. A method for assessing the tolerogenicity of a test peptide sequence, comprising the steps of:

5 (i) contacting a first cell population with said test peptide sequence,

(ii) contacting a second cell population with a control peptide sequence

10 (iii) determining whether IL-10 expression in each said cell population is increased, and optionally

(iv) correlating the result of step (iii) with the tolerogenicity of the test peptide sequence,

15 wherein each said cell population comprises mononuclear leukocytes from a donor previously infected by an infectious agent, and said control peptide sequence is derived from said infectious agent.

20 23. A method according to claim 22 wherein said control peptide sequence has previously been identified to induce IL-10 expression in a cell population comprising mononuclear leukocytes from a donor previously infected by said infectious agent.

25 24. A method according to claim 21 or claim 22, wherein said first and second cell populations are derived from the same donor.

30 25. A method according to claim 24, wherein said first and second cell populations comprise a T cell clone capable of proliferating in response to the control peptide.

26. A method according to any one of claims 22 to 25, wherein said infectious agent is EBV.

35 27. A method according to claim 26, wherein said control peptide is derived from LMP1 or LMP2.

28. A method according to claim 27, wherein said control peptide comprises one or more of P1 to P75 and P1' to P96'.

29. A method of tolerising a cell population to a target antigen,  
5 comprising contacting said cell population with

(a) a tolerogenic peptide sequence from an infectious agent, or a nucleic acid encoding said test peptide sequence, such that said test peptide sequence is expressed in said cell population; and  
10

(b) the target antigen, or a nucleic acid encoding said test peptide sequence, such that said test peptide sequence is expressed in said cell population;

15 wherein said cell population comprises mononuclear leukocytes from a subject seropositive for said infectious agent.

30. A method according to claim 29, comprising the steps of contacting a population of antigen presenting cells with said tolerogenic peptide sequence and said target antigen, and subsequently contacting said cell population with said population of antigen presenting cells.  
20

31. A method according to claim 29 or claim 30, wherein said mononuclear leukocytes are contacted with said tolerogenic peptide sequence and said target antigen *in vitro*.  
25

32. A method according to claim 31, wherein said cell population or a subset thereof is re-administered to said subject after contacting with said tolerogenic peptide sequence and said target antigen.  
30

33. A method according to claim 30, wherein said population of antigen presenting cells is contacted with said tolerogenic peptide sequence and said target antigen *in vitro* and said cell population is contacted with said population of antigen presenting cells *in vivo*.  
35

REPLACED BY  
ART 34 AMOT

60

34. A method according to claim 29, wherein said tolerogenic peptide sequence and said target antigen are administered directly to said subject.

35. A method according to any one of claims 29 to 34, wherein the infectious agent is a virus.

36. A method according to claim 35, wherein the virus is a herpesvirus encoding a viral IL-10 homologue.

37. A method according to claim 36, wherein the virus is EBV.

38. A method according to claim 37, wherein the tolerogenic peptide sequence is derived from EBV LMP1 protein or LMP2 protein.

39. A method according to claim 38, wherein the tolerogenic peptide sequence comprises one or more of the sequences P1 to P75 or P1' to P96'.

40. A pharmaceutical composition, for tolerising a subject against a target antigen, comprising a tolerogenic peptide sequence from an infectious agent, or a nucleic acid encoding a tolerogenic peptide sequence from an infectious agent, in admixture with a pharmaceutically acceptable carrier.

41. A pharmaceutical composition according to claim 40, wherein the tolerogenic peptide sequence is derived from EBV.

42. A pharmaceutical composition according to claim 41, wherein the tolerogenic peptide sequence is derived from LMP1 or LMP2.

43. A pharmaceutical composition according to claim 42, wherein the tolerogenic peptide sequence comprises one or more of the peptide sequences P1 to P75 or P1' to P96'.

44. A pharmaceutical composition according to any one of claims 40 to 43, further comprising said target antigen.

45. A pharmaceutical composition according to any one of claims 41 to 44, for administration to an individual previously infected with EBV.

46. Use of EBV LMP1, LMP2, or a fragment or mimetic thereof, or a nucleic acid encoding the same, in the preparation of a medicament for the prophylaxis or treatment of a condition mediated by an immune response directed against a target antigen.

47. Use according to claim 46, wherein the medicament is formulated for administration in conjunction with the target antigen or a nucleic acid encoding the target antigen.

48. Use according to claim 46 or 47, wherein the medicament comprises the target antigen or a nucleic acid encoding the target antigen.

49. Use according to any one of claims 46 to 48, wherein the condition is type I diabetes mellitus, coeliac disease, multiple sclerosis, rheumatoid arthritis, systemic lupus erythaematosus, myaesthesia gravis, autoimmune haemolytic anaemia, thrombocytopenia, an atopic response or allergy, or a response to a therapeutic product.

50. Use according to any one of claims 46 to 48 wherein the target antigen is a cell.

51. Use according to claim 50 wherein the cell is for transplantation.

52. Use according to claim 51 in combination with claim 48 wherein the cell comprises nucleic acid encoding the tolerogenic peptide sequence.

53. Use according to any one of claims 46 to 52 wherein the medicament is formulated for administration to an individual previously infected with EBV.

5 54. A peptide having the sequence of any one of P1 to P75 and P1' to P96'.

10 55. A peptide according to claim 54, having the sequence of any one of P2, P4, P5, P6, P7, P8, P9, P10, P12, P13, P14, P15, P16, P17, P18, P20, P22, P23, P24, P25, P26, P27, P29, P30, P32, P34, P35, P39, P68, P71, P72.